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10/665,722	09/19/2003	Victor Morozov	GMU-08-013U	4650
28598 7590 01/20/2010 GEORGE MASON UNIVERSITY OFFICE OF TECHNOLOGY TRANSFER, MSN 5G5 4400 UNIVERSITY DRIVE FAIRFAX, VA 22030			EXAMINER JUNG, UNSU	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/665,722

**Applicant(s)**

MOROZOV ET AL.

**Examiner**

UNSU JUNG

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 November 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 8.9.14-30 and 33-43 is/are pending in the application.
- 4a) Of the above claim(s) 8.9.14-20, 24-30 and 42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-23, 33-41 and 43 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-940)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election with traverse of species 1 (plasma, claim 41) in the reply filed on November 23, 2009 is acknowledged. The traversal is on the ground(s) that search may be carried out without an undue burden on the examiner as the specification discloses that plasma-treated surface can be made hydrophobic. Although plasma treatment can result in hydrophobic surface, plasma treatment can yield other types of surfaces and hydrophobic surface can be obtained via a different surface treatment means. Therefore, while searches would be expected to overlap, there is no reason to expect the searches to be coextensive.

The requirement is still deemed proper and is therefore made FINAL.

2. Elected species read on claims 21-23, 33-41, and 43. Claim 42 has been withdrawn from further consideration as it reads on non-elected species.

### ***Status of Claims***

3. As a preliminary matter, a typo has been noted in the previous Office Action dated November 9, 2009. On p2, amendments to claims 21 and 23 and addition of new claims 36-43 have been acknowledged. However, claim amendments further should include cancellation of claims 31 and 32. Accordingly, claims 8, 9, 14-30, and 33-43

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should be indicated pending and claims 21-23 and 33-43 should be indicated as being under consideration.

4. Claims 8, 9, 14-30, and 33-43 are pending, claims 8, 9, 14-20, 24-30, and 42 have been withdrawn from consideration, and claims 21-23, 33-41, and 43 are currently under consideration for patentability under 37 CFR 1.104.

#### ***Priority***

5. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The instant application, filed on September 19, 2003, claims the benefit of priority of U.S. Provisional Patent Application Serial No. 60/412,664, filed on September 20, 2002.

#### ***Rejections Withdrawn***

6. Rejection of claims 31 and 32 under 35 U.S.C. 112, first paragraph has been withdrawn in view of cancelled claims 31 and 32 in the reply filed on August 27, 2009.

#### ***Claim Objections***

7. Claim 40 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 40, which is

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dependent from claim 39, recites cyanoacrylate glue. Cyanoacrylate is genus encompassing different types of cyanoacrylates including species of octylcyanoacrylate as recited in claim 39. Since the scope of claim 40 is larger than the scope of its parent claim 39, claim 40 fails to further limit the subject matter of claim 39.

### ***New Grounds of Rejections***

#### ***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. The following prior art rejections has been modified (**bolded passages**) due to amendment of independent claim 21 and addition of new claims 36-41 and 43 in the reply filed on August 27, 2009.

12. Claims 21, 33, and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al. (U.S. Patent No. 6,245,508 B1, June 12, 2001) (hereinafter "Heller") in view of Goldstein et al. (U.S. Patent No. 4,584,075, Apr. 22, 1986) (hereinafter "Goldstein").

Heller teaches a method for detecting an analyte (see entire document) comprising:

- immobilizing a probe on a surface of a first semi-permeable membrane **that is positioned across a plurality of channels formed from wells of a microplate** (permeation layer, column 10, lines 5-9 and 17-40 and Fig. 2A), only the edges of the first semi-permeable membrane are bound to a first support and the immobilized probe molecule is placed in a channel comprising an analyte solution or suspension (column 10, line 66-column 11, line 2);

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- applying electric potential to the analyte to move the analyte toward the probe, thereby allowing the analyte to bind the probe (column 10, line 66-column 11, line 21);
- reversing the force or applying another force, to remove unbound or weakly bound analyte from the surface (column 11, lines 22-41); and
- detecting the analyte bound to the probe (column 10, lines 17-20 and column 18, line 3).

With respect to claim 33, Heller teaches that the surface is an activated surface (functionalized surface, column 18, lines 7-17) and that the surface is a semi-permeable membrane, penetrable for salt and buffer ions (small charged entities), but not for analytes (large charged entities, column 10, lines 5-9).

With respect to claims 35, Heller teaches multitude of the first semi-permeable membrane used in parallel (column 5, lines 22-32).

However, Heller fails to teach a method, further comprising the steps of placing a second semi-permeable membrane in a position that is parallel to the first semi-permeable membrane forming a gap with the first semi-permeable membrane, wherein the first probe molecules are inside the gap and facing the second semi-permeable membrane; contacting the side of the first semi-permeable membrane that is outside the gap with a first electrolyte solution, the first electrolyte solution being in contact with a first electrode; contacting the side of the second semi-permeable membrane that is outside the gap with a second electrolyte solution, the second electrolyte solution being in contact with a second electrode; and filling the gap with an analyte solution or

suspension to create a fluid connection between analytes in the analyte solution or the suspension with the first probe molecules.

Goldstein teaches a method for rapid binding of bioactive molecules to their ligands immobilized on a surface using electrophoretic transport of bioactive molecules (see entire document, particularly Fig. 1(b)). In the method of Goldstein, two barriers (semi-permeable membranes) in a position that is parallel to each other forming a gap between the two membranes (first and second semi-permeable membranes, column 4, line 59-column 5, line 45). A biospecific ligand attached to the barrier 3 in Fig. 1(b) (the first probe molecules are inside the gap and facing the second semi-permeable membrane). Each side of first and second barriers (sides of the semi-permeable membranes outside the gap, compartments 7 and 8 in Fig. 1(b)) are filled with appropriate electrolyte solutions and the gap (compartment 6 in Fig. 1(b)) is filled with appropriate liquid containing ligate(s) (analyte solution, column 4, line 59-column 5, line 45). The second barrier provides protection of the sorbing groups 5 and/or ligands sorbed thereon or desorbed therefrom from the products of electrolysis as electrode (column 3, lines 3-14).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ the second semi-permeable membrane in a position that is parallel to each of the first semi-permeable membrane to form a gap with the first semi-permeable membrane as taught by Goldstein (which further teaches that the first probe molecules are inside the gap and facing the second semi-permeable membrane and further includes steps of contacting the side of the first semi-permeable



membrane that is outside the gap with a first electrolyte solution, the first electrolyte solution being in contact with a first electrode; contacting the side of the second semi-permeable membrane that is outside the gap with a second electrolyte solution, the second electrolyte solution being in contact with a second electrode; and filling the gap with an analyte solution or suspension to create a fluid connection between analytes in the analyte solution or the suspension with the first probe molecules) in the method of Heller in order to provide rapid binding of analytes to the probe molecules on the first membrane. The advantage of protecting of the probe molecules and/or analytes thereon from the electrodes provides the motivation to combine teachings of Heller and Goldstein with reasonable expectation of success.

13. Claims 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (U.S. Patent No. 6,245,508 B1, June 12, 2001) in view of Goldstein (U.S. Patent No. 4,584,075, Apr. 22, 1986) as applied to claim 21 above, and further in view of Baselt (U.S. Patent No. 5,981,297, Nov. 9, 1999).

Heller in view of Goldstein teaches a method for detecting an analyte as set forth above. Although Heller teaches that variety of different detection methods can be employed using appropriate labeling/reporter groups that produce detectable signal (column 19, line 47-column 20, line 6), Heller in view of Goldstein is silent on teaching the analyte bound to a particle.

With respect to claims 22 and 23, Baselt teaches method and apparatus for detecting target molecules in a liquid phase (see entire document, particularly Abstract).

The apparatus monitors whether the target molecule has selectively bound to recognition agents on the surface of a magnetic field sensor by monitoring the output of the sensor (Abstract). The recognition agents which selectively bind target molecules are covalently bound to microfabricated magnetic field sensors (Abstract). These sensors are then exposed to a sample suspected of containing the target molecules, whereupon the recognition agents bind to and immobilize any target molecules present (Abstract). A change in the output of the magnetic field sensors indicates the presence of magnetic particles bound to the sensors, and thereby indicates the presence and concentration of target molecule in the sample (Abstract). The method of Baselt allows simultaneous and rapid detection of a wide range of chemical and biological species obtained from either the vapor or liquid phase, with a high degree of sensitivity (column 3, lines 16-35). The detection device of Baselt is compact and fully automated and allows measurement of intermolecular binding forces and thereby analyze recognition events (column 3, lines 16-35).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ the detection method of Baselt, in which analytes are bound to magnetic particles, in the method of Heller in view of Goldstein as the detection method of Baselt allows simultaneous and rapid detection of a wide range of chemical and biological species obtained from either the vapor or liquid phase, with a high degree of sensitivity. The advantage of allowing simultaneous and rapid detection of a wide range of chemical and biological species obtained from either the vapor or liquid phase, with a high degree of sensitivity using compact and fully automated device

further allowing measurement of intermolecular binding forces and thereby analyze recognition events provides the motivation to combine methods of Heller view of Goldstein and Baselt. Further, one of ordinary skill in the art would have had a reasonable expectation of success in employing the detection method of Baselt, in which analytes are bound to magnetic particles, in the method of Heller view of Goldstein since Heller teaches that variety of different detection methods known in the art can be employed using appropriate labeling/reporter groups that produce detectable signal.

14. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (U.S. Patent No. 6,245,508 B1, June 12, 2001) in view of Goldstein (U.S. Patent No. 4,584,075, Apr. 22, 1986) as applied to claim 21 above, and further in view of Bier (U.S. Patent No. 4,040,940, Aug. 9, 1977).

Heller in view of Goldstein teaches a method for detecting an analyte as set forth above. Although Heller in view of Goldstein teaches that the analyte solutions may be delivered to the reaction sites via electrophoretic flow in the gap (polarization of membrane), Heller in view of Goldstein is silent on teaching an additional step of forming a self-forming density gradient in the channel in order to suppress convection in the channel.

Bier teaches that the electrophoretic process of separation of soluble or particulate ionized matter is potentially complicated by convective effects (see entire document, particularly column 1, lines 16-33). These may be caused by unequal

temperature distribution, due to Joule heating or unequal solute concentration, due to resolution of the sample into sharply compartmentalized individual zones. Stabilization against these convective disturbances is essential. The most common way to avoid convection is to work in gels, or columns packed with finely dispersed matter, such as glass beads, agarose granules, starch granules, etc., whereby electrophoresis is carried out in the interstitial capillary bed formed by these materials. Another way to stabilize against convective flow is to create a density gradient using an inert solute, such as sucrose (self-forming density gradient).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to provide a density gradient using an inert solute, such as sucrose (self-forming density gradient) as taught by Bier in the channel of Heller in view of Goldstein in order to stabilize against convective flow during the electrophoretic flow of the analyte solution within the channel. The advantage of avoiding the convective flow, which can potentially complicate the electrophoretic flow of particles/analytes in solution, provides the motivation to combine teachings of Heller in view of Goldstein and Bier with a reasonable expectation of success.

**15. Claims 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (U.S. Patent No. 6,245,508 B1, June 12, 2001) in view of Goldstein (U.S. Patent No. 4,584,075, Apr. 22, 1986) as applied to claim 21 above, and further in view of Dyson et al. (U.S. Patent No. 4,889,606, Dec. 26, 1989) (hereinafter "Dyson").**

Heller in view of Goldstein teaches a method for detecting an analyte as set forth above. Although Heller in view of Goldstein teaches that the analyte solutions may be delivered to the reaction sites via electrophoretic flow in the gap (polarization of membrane), Heller in view of Goldstein is silent on teaching an additional step of deflecting bubbles with a frame having a porous membrane.

Dyson teaches a well known phenomenon; in which gases are produced at electrodes when a current flows through a conducting liquid (see entire document, particularly column 10, lines 14-28). It is inevitable that the bubbles will rise and this may be a problem for the bubbles released from a lower electrode (column 10, lines 14-28). These bubbles may accumulate and so interfere with the electric field generated thereby creating local areas of low and high field strength (column 10, lines 14-28). To get round this problem a third porous plate (not shown) could be inserted between the lower electrode and the porous plate (column 10, lines 14-28). The third porous plate could be tilted diagonally so as to deflect the bubbles and transfer them to some non-interfering area whilst itself having no detrimental effect on the electric fields generated (column 10, lines 14-28).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to porous plate (a frame having a porous membrane) of Dyson in the method of Heller in view of Goldstein in order to deflect bubbles that may accumulate within the electrolyte solution. The advantage of deflecting bubbles that may interfere with electric field being

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generated by electrodes provides the motivation to combine teachings of Heller in view of Goldstein and Dyson with a reasonable expectation of success.

With respect to claim 37, Dyson teaches that the porous plate can be placed at an angle (column 10, lines 14-28), but is silent on teaching the specific range of angles from about 30 to about 50° relative to the microplate. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable. Section 2144.05 [R3] of the MPEP presents case law upholding obviousness rejections based on optimization of ranges:

**A. Optimization Within Prior Art Conditions or Through Routine Experimentation**

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.)

The specification discloses the appropriate ranges that apply to the

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claimed invention on page(s) 39 as 30-50°. However, the specification does not disclose that the specifically claimed range(s) of 30-50° is for any particular purpose or to solve any stated problem that distinguishes it from the other ranges disclosed. The specification therefore lacks disclosure of the criticality required by the Courts in providing patentability to the claimed range(s).

In addition to a lack of disclosed criticality in the specification, an obviousness rejection based upon optimization must rely on prior art that discloses the optimized parameter is a result-effective variable. See MPEP 2144.05:

**B. Only Result-Effective Variables Can Be Optimized**

A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq. ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result-effective variable.). See also *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) (prior art suggested proportional balancing to achieve desired results in the formation of an alloy).

Since *Heller* in view of *Goldstein* and *Dyson* teaches that the porous plate can be placed at an angle (column 10, lines 14-28 of *Dyson*), the prior art therefore provides teaching that the angle of the porous plate with respect to the microplate is a variable that achieves a recognized result, and satisfies the above requirement of a result-effective variable in order to set forth an obviousness rejection based on optimization.

Because Applicants fail to disclose that the claimed range(s) of 30-50° provides a criticality to the invention that separates it from the other ranges in the specification, and the prior art discloses the porous plate can be placed at an angle absent unexpected results, it would therefore have been obvious for one of ordinary skill to discover the optimum workable range(s) of 30-50° by normal optimization procedures known in the arts.

16. Claims 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (U.S. Patent No. 6,245,508 B1, June 12, 2001) in view of Goldstein (U.S. Patent No. 4,584,075, Apr. 22, 1986) as applied to claim 21 above, and further in view of Lazar (U.S. Patent No. 5,290,825, Mar. 1, 1994).

Heller in view of Goldstein teaches a method for detecting an analyte as set forth above. Although Heller in view of Goldstein teaches that the first and second semi-permeable membranes are bound to first and second supports, respectively, Heller in view of Goldstein fails to teach that the first and second semi-permeable membranes are bound to first and second supports via glue such as octylcyanoacrylate glue.

Lazar teaches known adhesives/glues such as cyanoacrylates including octylcyanoacrylate (see entire document, particularly column 1, lines 35-40).

The rationale to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known



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methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art.

*KSR International Co. v. Teleflex Inc.*, 550 U.S. at \_\_\_, 82 USPQ2d at 1395;

*Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282, 189 USPQ 449, 453 (1976);

*Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 62-63, 163

USPQ 673, 675 (1969); *Great Atlantic & P. Tea Co. v. Supermarket Equipment*

*Corp.*, 340 U.S. 147, 152, 87 USPQ 303, 306 (1950). "[I]t can be important to

identify a reason that would have prompted a person of ordinary skill in the

relevant field to combine the elements in the way the claimed new invention

does." *KSR*, 550 U.S. at \_\_\_, 82 USPQ2d at 1396.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ any of the well known glues/adhesive such as cyanoacrylates including octylcyanoacrylate as taught by Lazar in order to bind the semi-permeable membranes to their supports in the method of Heller in view of Goldstein. The combination would have yielded nothing more than predictable results to one of ordinary skill in the art since the use of known glue/adhesive composition to bind two different elements with no change in their respective functions.

17. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (U.S. Patent No. 6,245,508 B1, June 12, 2001) in view of Goldstein (U.S. Patent No. 4,584,075, Apr. 22, 1986) as applied to claims 21 and 33 above, and

further in view of Hsu et al. (U.S. Patent No. 5,028,657, July 2, 1991) (hereinafter "Hsu").

Heller in view of Goldstein teaches a method for detecting an analyte as set forth above. Although Heller teaches that permeation layer may be formed from polymeric materials (column 17, line 64-column 18, line 6) and the surface layer can be functionalized with different capture probes such as DNA and proteins (column 5, lines 22-47 and column 18, lines 36-42), Heller in view of Goldstein is silent on teaching that the surface layer is activated with plasma.

Hsu teaches that plasma activation can be used to immobilize proteins on polymeric matrix regardless of the form of the surface (see entire document, particularly column 1, lines 54-64). The plasma activation method can be used to immobilize a wide range of proteins using substantially the same technique (column 1, lines 24-27). Protein membrane having good activity and stability can be produced using the plasma activation method (column 1, lines 47-53).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to employ the plasma activation method of Hsu in the method of Heller in view of Goldstein in order to activate the surface layer for subsequent protein probe immobilization. The advantage of being able to immobilize a wide range of proteins using substantially the same technique resulting in protein membranes having good activity and stability provides the motivation to combine teachings of Heller in view of Goldstein and Hsu with a reasonable expectation of success.

18. Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (U.S. Patent No. 6,245,508 B1, June 12, 2001) in view of Goldstein (U.S. Patent No. 4,584,075, Apr. 22, 1986) and Baselt (U.S. Patent No. 5,981,297, Nov. 9, 1999) as applied to claim 22 and 23 above, and further in view of Kurahashi et al. (JP 63315115A, Dec. 22, 1988 (hereinafter "Kurahashi")).

Heller in view of Goldstein and Baselt teaches a method for detecting an analyte as set forth above. Although Baselt teaches that non-specifically bound label particles can be moved using magnetic force (claims 14 and 15), Heller in view of Goldstein and Baselt fails to teach that particles are moved using centrifugal forces.

Kurahashi teaches that magnetic particles can be removed by means of centrifugal force (Abstract).

Because magnetic particles can be removed by using both magnetic and centrifugal forces, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute one method for the other to achieve the predictable result of removing magnetic particles.

#### ***Response to Arguments***

19. Rejection of claims 21, 33, and 35 under 35 U.S.C. 103(a) as being unpatentable over Heller in view of Goldstein

Applicant's arguments filed on August 27, 2009 have been fully considered but they are not persuasive essentially for the reasons of record and arguments addressed herein.

Applicant's argument that the cited prior art do not recreate the claimed invention specifically the additional limitations seen in the amended claims has been fully considered but is not found persuasive in view of the previously stated grounds of rejection. As stated above, Heller teaches a first semi-permeable membrane that is positioned across a plurality of channels formed from wells of a microplate (permeation layer, column 10, lines 5-9 and 17-40 and Fig. 2A). Therefore, the prior art teachings of Heller and Goldstein do teach claimed invention including the additional limitations (a first semi-permeable membrane that is positioned across a plurality of channels formed from wells of a microplate) seen in the amended claims.

In view of the foregoing, the rejection of claims 21, 33, and 35 under 35 U.S.C. 103(a) as being unpatentable over Heller in view of Goldstein has been maintained.

20. Rejection of claims 22 and 23 under 35 U.S.C. 103(a) as being unpatentable over Heller in view of Goldstein, and further in view of Baselt

Applicant's arguments filed on August 27, 2009 have been fully considered but they are not persuasive essentially for the reasons of record and arguments addressed above.

In view of the foregoing, the rejection of claims 22 and 23 under 35 U.S.C. 103(a) as being unpatentable over Heller in view of Goldstein, and further in view of Baselt has been maintained.

21. Rejection of claim 34 under 35 U.S.C. 103(a) as being unpatentable over Heller in view of Goldstein, and further in view of Bier

Applicant's arguments filed on August 27, 2009 have been fully considered but they are not persuasive essentially for the reasons of record and arguments addressed above.

In view of the foregoing, the rejection of claim 34 under 35 U.S.C. 103(a) as being unpatentable over Heller in view of Goldstein, and further in view of Bier has been maintained.

22. Applicant's arguments with respect to claims 36-41 and 43 have been considered but are moot in view of the new ground(s) of rejection.

23. Since the prior art fulfills all the limitations currently recited in the claims, the invention as currently recited would read upon the prior art.

***Conclusion***

24. No claim is allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to UNSU JUNG whose telephone number is (571)272-8506. The examiner can normally be reached on M-F: 9-5.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Unsu Jung/  
Unsu Jung  
Primary Examiner  
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